

Creutzfeldt-Jakob Disease: Disinfection and Sterilization

Dr. William Rutala, University of North Carolina

A Webber Training Teleclass

CJD: Disinfection and Sterilization Issues

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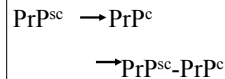
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Disinfection and Sterilization for Prion Diseases Topics

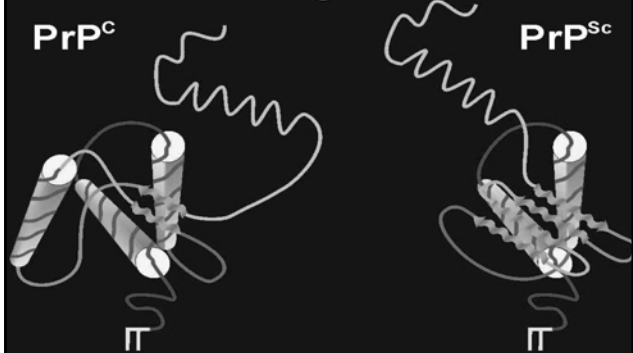
- Epidemiology and historical perspective
- Rationale for newer recommendations
 - Epidemiological studies of prion transmission
 - Infectivity of human tissues
 - Efficacy of removing microbes/proteins by cleaning
 - Prion inactivation studies
 - Risk associated with instruments
- Recommendations to prevent cross-transmission from medical devices contaminated with prions

Prion Diseases

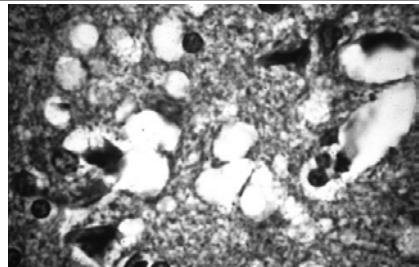
- Etiology
 - Prions (proteinaceous infectious agent)
 - ◆ No agent-specific nucleic acid
 - ◆ Host protein (PrP^c) converts to pathologic isoform (PrP^{sc}); PrP gene resides on chromosome 20
 - ◆ Mutation in this gene may trigger transformation
 - ◆ Accumulates in neural cells, disrupts function
 - ◆ Resistant to conventional D/S procedures



Structural Changes Occur in PrP



CJD



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Prion Diseases of Humans

- Kuru
- Gertsmann-Straussler-Scheinker (GSS)
- Fatal Familial Insomnia (FFI)
- Creutzfeldt-Jakob Disease (CJD)
- Variant CJD (vCJD), 1994 (March 2002, 115 cases)

**Prion Diseases
Animals**

- Scrapie in sheep and goats
- Transmissible mink encephalopathy
- Exotic ungulate encephalopathy
- Chronic wasting disease (elk, deer)
- Feline spongiform encephalopathy
- Bovine spongiform encephalopathy

Epidemiology of CJD in the US

- Degenerative neurologic disorder
- Incidence
 - One death/million population
 - No seasonal distribution, no geographic aggregation
 - Both genders equally affected
 - Age range 50-80+ years, average 67
- Long incubation disease (years)
- Rapid disease progression after onset (death within 6 mo)

Clinical Features of CJD

- Progressive dementia (memory, intellect, personality)
- Progressive motor deterioration
 - Unsteadiness and clumsiness
 - Visual deterioration
 - Muscle twitching
 - Severe dementia, mute, immobile
- Death (< 1 year)

Diagnosis of CJD

- Clinical syndrome
 - Progressive intellectual and neurological deterioration
- EEG-classic periodic triphasic wave
- MRI-hyperlucency in the putamen
- CSF testing (surrogate markers-14-3-3 [sensitivity/specificity >90% in the presence of typical clinical picture], tau protein)
- Neuropathology
 - Brain biopsy (dx in 95% of cases confirmed by autopsy)
 - Autopsy, neuropathology confirmation

vCJD and BSE Caused by Same Prion



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vCJD Caused by Exposure to Contaminated Bovine (brain and spinal cord in processed meats)



Variant CJD

- Strongly associated with epidemiology of BSE (1983) in UK
- BSE amplified by feeding cattle meat and bone meal infected with scrapie and/or BSE (rendering process changed in late 1970s, exposure to BSE (1984-1986), vCJD (1994-1996))
- June 2003, 144 cases vCJD (135 in UK, 6 in France, 1 Italy, Canada, US)
- Affects young persons (range 13-48y, median 28y)
- Clinical course is longer (13 mo)
- vCJD and BSE not reported in the United States (April 2002, 1 case of vCJD reported in Florida in person emigrated from UK)
- vCJD and BSE are believed to be caused by the same prion agent

BSE (Bovine Spongiform Encephalopathy) United Kingdom, 1986 - 2000

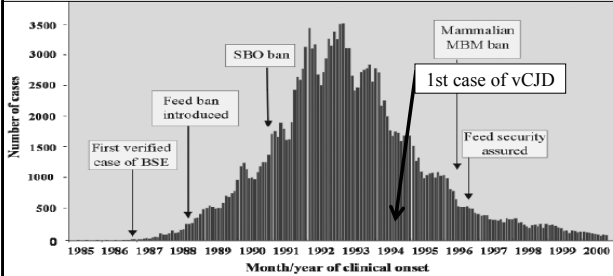
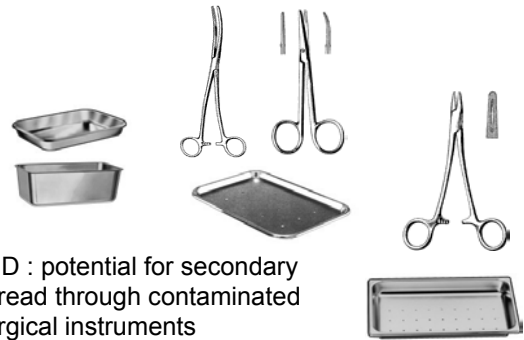


Figure. Time course of epidemic bovine spongiform encephalopathy in the United Kingdom, 1986-2000, with dates of major precautionary interventions. The mammalian ban on meat and bone meal in March 1996 extended the 1994 ban for farmed feed animal species to include all mammalian species.



CJD : potential for secondary spread through contaminated surgical instruments

CJD: DISINFECTION AND STERILIZATION Historical Perspective

- CJD exhibit an unusual resistance to conventional chemical and physical decontamination methods
- Until recently, all medical/surgical instruments from CJD patients received special prion reprocessing
- Draft guidelines of the CDC (Favero, 1995) suggested a risk assessment consider cleaning and prion bioburden on instruments that results from contact with infectious tissues

Decreasing Order of Resistance of Microorganisms to Disinfectants/Sterilants

- Prions
- Spores
- Mycobacteria
- Non-Enveloped Viruses
- Fungi
- Bacteria
- Enveloped Viruses

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CJD: DISINFECTION AND STERILIZATION

- Rationale for newer recommendations
 - Epidemiological studies of prion transmission
 - Epidemiological studies of prion transmission via surgical instruments
 - Infectivity of human tissues
 - Efficacy of removing microbes/proteins by cleaning
 - Prion inactivation studies
 - Risk associated with instruments
- Recommendations

Transmissibility of Prions

- Transmission
 - Not spread by contact (direct, indirect, droplet) or airborne
 - Not spread by the environment
 - Experimentally-all TSEs are transmissible to animals, including the inherited forms
 - Epidemiology of CJD: sporadic-85%; familial-15%; iatrogenic-1% (primarily transplant of high risk tissues, ~200 cases worldwide)

**Risk of CJD Transmission
Blood**

- Lack of epidemiologic evidence includes:
 - CJD not found in patients with hemophilia
 - Intravenous drug use does not increase the risk
 - Tracking of blood donated by those in whom CJD subsequently developed has not uncovered the disease in recipients
 - Failure to induce CJD in chimpanzees when transfused with full units of blood from CJD patients

Transmission of CJD to HCWs

- No confirmed cases of transmission to HCWs
 - Cases have been reported in nurses, orthopedic surgeons, neurosurgeons, etc
 - No excess
- No cases reported in CJD researchers
 - Exposure to infected brains and long-term exposures

Iatrogenic Transmission of CJD

- Contaminated medical instruments
 - Electrodes in brain (2)
 - Neurosurgical instruments in brain (4?)
- Implantation of contaminated grafts
 - Dura mater grafts (114)
 - Corneal grafts (2)
- Use of human growth hormone (139) and gonadotropin (4)

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CJD and Medical Devices

- Six cases of CJD associated with medical devices
 - 2 confirmed cases-depth electrodes; reprocessed by benzene, alcohol and formaldehyde vapor
 - 4 cases-CJD following brain surgery, index CJD identified-1, suspect neurosurgical instruments
- Cases occurred before 1980 in Europe
- No known cases since 1980 and no known failure of steam sterilization

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Risk of CJD Transmission

- Epidemiologic evidence (eye, brain) linking specific body tissue or fluids to CJD transmission
- Experimental evidence in animals demonstrating that body tissues or fluids transmit CJD
 - Infectivity assays a function of the relative concentration of CJD tissue or fluid

Risk of CJD Transmission

Risk of Infection	Tissue
High	Brain (including dura mater), spinal cord, and eye
Low	CSF, liver, lymph node, kidney, lung, spleen, placenta, olfactory epithelium
No	Peripheral nerve, intestine, bone marrow, whole blood, leukocytes, serum, thyroid gland, adrenal gland, heart, skeletal muscle, adipose tissue, gingiva, prostate, testis, tears, nasal mucus, saliva, sputum, urine, feces, semen, vaginal secretions, and milk

High-transmission to inoc animals >50%; Low-transmission to inoc animals >10-20% but no epid evidence of human inf

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CJD: DISINFECTION AND STERILIZATION

- Effectiveness must consider both removal by cleaning and inactivation
 - Probability of a device remaining capable of transmitting disease depends on the initial contamination and effectiveness of C/D/S.
 - Cleaning results in a 4 log₁₀ reduction of microbes and ~2 log₁₀ reduction in protein contamination

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Decreasing Order of Resistance of Microorganisms to Disinfectants/Sterilants

Prions
Spores
Mycobacteria
Non-Enveloped Viruses
Fungi
Bacteria
Enveloped Viruses

**Ineffective or Partially-Effective Disinfectants:
CJD**

- Alcohol
- Ammonia
- Chlorine dioxide
- Formalin
- Glutaraldehyde
- Hydrogen peroxide
- Iodophors/Iodine
- Peracetic acid
- Phenolics

**CJD: Ineffective or Partially Effective Disinfectants
Examples**

- Glutaraldehyde (5%)
 - Partially effective
- Iodine (2%)
 - ~1 log decrease in 30m
- Hydrogen peroxide (3%)
 - ~ 1 log decrease in 60m
- Formaldehyde (3.7%)
 - ~ 1 log decrease in 60m

**Ineffective or Partially Effective Processes:
CJD**

- Gases
 - Ethylene oxide
 - Formaldehyde
- Physical
 - Dry heat
 - UV
 - Microwave
 - Ionizing
 - Glass bead sterilizers
 - Autoclave at 121°C, 15m

Effective Disinfectants
(≥4 log₁₀ decrease in LD₅₀ with 1 hour)

- Sodium hydroxide
 - 1 N for 1h (variable results)
- Sodium hypochlorite
 - 5000 ppm for 15m
- Guanidine thiocyanate
 - 4M
- Phenolic (LpH)
 - 0.9% for 30m

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Effective Processes: CJD

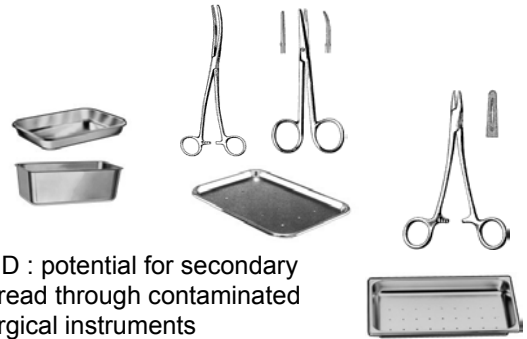
- Autoclave
 - 134°C-138°C for 18m (prevacuum)
 - 132°C for 60m (gravity)
- Combination (chemical exposure then steam autoclave, potentially deleterious to staff, instruments, sterilizer)
 - Soak in 1N NaOH, autoclave 134°C for 18m
 - Soak in 1N NaOH, autoclave 121°C for 30m

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Disinfection and Sterilization

- EH Spaulding believed how an object will be D/S depended on the objects intended use
 - CRITICAL-objects that enter normally sterile tissue or the vascular system should be sterile
 - SEMICRITICAL-objects that touch mucous membranes or skin that is not intact requires a disinfection process (high level disinfection) that kills all but bacterial spores (prions?)
 - NONCRITICAL-objects that touch only intact skin require low-level disinfection



Risk Assessment: Patient, Tissue, Device

- Patient
 - Known or suspected CJD or other TSEs
 - Rapidly progressive dementia
 - Familial history of CJD, GSS, FFI
 - History of dura mater transplant, cadaver-derived pituitary hormone injection
- Tissue
 - High risk-brain, spinal cord, eyes
- Device
 - Critical or semicritical

Risk Assessment

- High risk patient-certain patients capable of transmitting infection.
- High risk tissue-CJD can be transmitted to laboratory animals by inoculation of infective material. Iatrogenic episodes of CJD have been associated with these infective materials.
- High risk devices-risk of infection associated with the use of the device.

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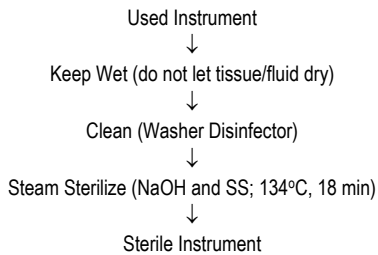
CJD: Recommendations for Disinfection and Sterilization

- High risk patient, high risk tissue, critical/semicritical device-special prion reprocessing (Category IB)
- High risk patient, **low/no risk tissue**, critical/semicritical special prion reprocessing (Category II)
- **Low risk patient**, high risk tissue, critical/semicritical device-conventional D/S
- High risk patient, high risk tissue, **noncritical device**-conventional disinfection

CJD: Disinfection and Sterilization Conclusions

- Cleaning with special prion reprocessing
 - NaOH and steam sterilization (e.g., 1N NaOH 1h, 121°C 30 m)
 - 134°C for 18m (prevacuum)
 - 132°C for 60m (gravity)
- No low temperature sterilization technology effective
- Four disinfectants (e.g., chlorine) effective (4 log decrease in LD₅₀ within 1h)

CJD: Sterilization in Health Care

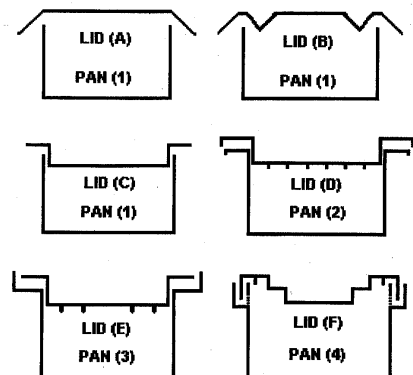


CJD: Instrument Reprocessing

- High Risk Tissue, High Risk Patient, Critical/Semicritical Device-special prion reprocessing
 - Steam autoclave cleaned instrument
 - ◆ 134°C for ≥18m (prevacuum, porous)
 - ◆ 132°C for 1h (gravity)
 - Instruments that are difficult to clean
 - ◆ Soak 1h in 5,000ppm chlorine or 1N NaOH
 - ◆ Rinse, clean and autoclave as above

CJD: Instrument Reprocessing

- Special prion reprocessing by combination of NaOH and steam sterilization
 - Immerse in 1N NaOH for 1 hour; remove and rinse in water, then transfer to an open pan and autoclave for 1 hour
 - Immerse in 1N NaOH for 1 hour and heat in a gravity displacement sterilizer at 121°C for 30 minutes
- Combined use of autoclaving in sodium hydroxide has raised concerns of possible damage to autoclaves, and hazards to operators due to the caustic fumes.
- Risk can be minimized by the use of polypropylene containment pans and lids (AJIC 2003; 31:257-60).



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CJD: Instrument Reprocessing

- **Low/No Risk Tissue**, High Risk Patient, Critical/Semicritical Device
 - These devices can be cleaned and disinfected or sterilized using conventional protocols of heat or chemical sterilization, or high-level disinfection (HLD for semicritical)
 - Endoscopes would be contaminated only with low risk materials and hence standard cleaning and HLD protocols would be adequate

CJD: Environmental Surfaces

- High/Low/No Risk Tissue, High Risk Patient, **Noncritical Surface/Device**
 - Environmental surfaces contaminated with high risk tissues (autopsy table in contact with brain tissue) should be cleaned and then spot decontaminated with a 1:10 dilution of bleach
 - Environmental surfaces contaminated with low/no risk tissue require only routine disinfection

D/S of Medical Devices

General Comments

- Issues
 - Do not allow tissue/body fluids to dry on instruments (e.g., place in liquid)
 - Some decontamination procedures (e.g., aldehydes) fix protein and this may abolish effectiveness of autoclaving
 - Clean instruments but prevent exposure
 - Assess risk of patient, tissue, device
 - Choose effective process

**CJD
General Precautions**

- High Risk CJD Patient
- Standard precautions apply
- No special precautions for processing laundry, food utensils, medical waste or disposal of body fluids
- Should not serve as donor of organ/tissue/blood

Prevent Patient Exposure to CJD Contaminated Instruments

How do you prevent patient exposure to neurosurgical instruments from a patient who is latter given a diagnosis of CJD?

Hospitals should use the special prion reprocessing precautions (Neurosurgery contacts IC, Pathology, Central Processing) for instruments from patients undergoing brain biopsy when a specific lesion (e.g. tumor) has not been demonstrated (e.g., CT, MRI). Alternatively, neurosurgical instruments used in such cases could be disposable.

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Disinfection and Sterilization for Prion Diseases

Topics

- Epidemiology and historical perspective
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vCJD: Disinfection and Sterilization

- To date no reports of human-to-human transmission of vCJD by blood or tissue
- Unlike CJD, vCJD detectable in lymphoid tissues and prior to onset of clinical illness
- Special prion reprocessing (or single use instruments) proposed in the UK in dental, eye, or tonsillar surgery on high risk patients for CJD or vCJD
- If epidemiological and infectivity data show these tissues represent a high transmission risk then special prion reprocessing could be extended to these procedure

Inactivation of Prions

Recent Studies

- Yan et al. Infect Control Hosp Epidemiol 2004;25:280.
- Fichet et al. Lancet 2004;364:521.
- Baier et al. J Hosp Infect 2004;57:80.
- Lemmer et al. J Gen Virol 2004;85:3805.
- Jackson et al. J Gen Virol 2005;86:869.
- Race R and Raymond G. J Virol 2004;78:2164.

Prion Inactivation Studies

- Problems
 - Investigators used aliquots of brain tissue macerates vs. intact tissue (smearing, drying); weights of tissue (50mg-375mg)
 - Studies do not reflect reprocessing procedures in a clinical setting (e.g., no cleaning)
 - Factors that affect results include: strain of prion (22A), prion conc in brain tissue, animal used, exposure conditions, validation and cycle parameters of sterilizers, resistant subpopulation, different test tissues, different duration of observations, screw cap tubes with tissue (air), etc

Conclusions

- Epidemiologic evidence suggests nosocomial CJD transmission via medical devices is very rare
- Guidelines based on epidemiologic evidence, tissue infectivity, risk of disease via medical devices, and inactivation data
- Risk assessment based on patient, tissue and device
- Only critical/semicritical devices contacting high risk tissue from high risk patients require special prion reprocessing

Thank you

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Disinfection and Sterilization for Prion Diseases

References

- Rutala WA, Weber DJ. Creutzfeldt-Jakob Disease: Recommendations for Disinfection and Sterilization. Clin Inf Dis 2001;32:1348-1356.
- Rutala WA, Weber DJ, and HICPAC. Guideline for Disinfection and Sterilization (draft). Fed Reg. In press
- Rutala WA, Weber DJ. Disinfection and Sterilization in Health Care Facilities: What Clinician Need to Know. Clin Inf Dis 2004; 39:702-709.
- Prusiner SB. Prion Biology and Diseases. 1999. Cold Spring Harbor Laboratory Press, New York.

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